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WHAT IS CLAIMED IS:

1. A protein having a formula selected from the group consisting of: $R_1 - R_2$, $R_2 - R_1$, $R_1 - L_1 - R_2$, and $R_2 - L_1 - R_1$, wherein R_1 is a Fc protein, or variant or fragment thereof, R_2 is an OPG protein, or variant or fragment thereof, and L is a linker.

- 2. The protein of Claim $\frac{1}{2}$ having the 10 formula R_2 -L- R_1 .
 - 3. The protein according to claim 1, wherein the Fc protein is selected from the group consisting of:

(a) the Fc amino acid sequences as set forth in Figure 1; (560)

- (b) the amino acid sequence of subpart (a) having a different amino acid substituted or deleted in one or more of the following positions (using the numbering according to Figure 1):
 - (i) one or more cysteine residues;
 - (ii) one or more tyrosine residues;

(iii) cysteine at position 5 deleted or substituted with an alanine;

- (iv) leucide at position 20 deleted or substituted with glutamine;
- (v) glutamic acid at position 103 deleted or substituted with an alanine;
- (vi) lysine at position 105 deleted or substituted with an alanine;

(vii) lysine at position 107 deleted or substituted with an alanine;

(viii) deletion or substitution of one or more of the amino acids at positions 1, 2, 3, 4, and 5;

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	(ix) one or more residues substituted or
	deleted to ablate the Fc receptor binding site;
	(x) one or more residues substituted or
	deleted to ablate the complement (C1/q) binding
5	site; and
	(xi) a combination of subparts i-x;
	(c) the amino acid sequence of subparts (a)
	or (b) having a methionyl residue at the
	N-terminus;
10	(d) the Fc protein, or variant, fragment or
	derivative thereof, of any of subparts (a) through
	(c) comprised of a chemical moiety connected to
	the protein moiety;
	(e) a derivative of subpart (d) wherein said
15	chemical moiety is a water soluble polymer moiety;
	(f) a derivative of subpart (e) wherein said
	water soluble polymer modety is polyethylene
	glycol; and
	(g) a derivative of subpart (e) wherein said
20	water soluble polymer moiety is attached at solely
	the N-terminus of said protein moiety.
	4 The mark of a consider to glaim 1
	4. The protein according to claim 1,
25	wherein the OPG protein or variant, fragment or
25	derivative thereof, is/selected from the group
	consisting of: (a) the amino acid sequence 22-X wherein X
	is any residue from position 185 to 401 inclusive
٠٨.	as shown in Figure 2 (SEQ ID NO: 2);
% 30	(b) the amino acid sequence 22-X wherein X
30	is any residue from position 185 to 293 inclusive
	as shown in Figure 2 (SEQ ID NO: <u>A</u>);
4	(c) the amino acid sequence of subparts (a)
	and (h) having a mothional residue at the

N-terminus.

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(c) the OPG protein, or variant, fragment or derivative thereof, of any of subpart/s (a),(b) and (c) comprised of a chemical moiety connected to the protein moiety;

- (d) a derivative of subpart (c) wherein said chemical moiety is a water soluble polymer moiety;
- a derivative of subpart (d) wherein said water soluble polymer moiety is polyethylene glycol;
- A derivative of subpart (d) wherein said (f) water soluble polymer moiety is a polyamino acid moiety; and
- a derivative of subpart (d) wherein said (q) water soluble polymer moiety is attached at solely the N-terminus of said protein moiety.
- The protein of claim 1 wherein the 5. linker is one or more amino/acids selected from the group consisting of glycine, asparagine, serine, threonine and alanine.
- The protein of claim 1 wherein the 6. linker is selected from the group consisting of:

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a∤a-ala-ala;
(a)
         ala-ala-ala-ala;
(b)
         ala-ala-ala-ala-ala; (SCOID NOSZ)
(C)
(d)
         gly-gly-gly;
(e)
         gly-gly-gly-gly;
(f)
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ser-gly-gly-gly-gly-gly-gly-

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	(1)	gly-gly-ser-gly-	ser-ala-gly-ser-	
	(1) gly-ser-gly-gly-gly	-ser-gly-ser-gly-	(280 TONO:2)	
	(m)	a chemical moiet	,	
	(n)	any combination	of subparts (a)	
5	through (m).			
	7. A fu	sion protein comp	rising the amino	
	acid sequence selec	ted from the grow	p consisting of the	е
	amino acid sequence			
10	(SEQ ID NOS: 5 , 6	, <u>1</u> , <u>8</u> , respect	cively).	
		/	ice encoding for a	
	protein having the	/		
	consisting of: R ₁ -R	,		1
15	R ₁ is a Fc protein,	,		
	is an OPG protein,	or variant or fra	igment thereof, and	
	L is a linker.			
	9. The	nuclei¢ acid sequ	uongo of Claim 8	
20	encoding for a prot			
20	variant, fragment o	1		
	the group consistin	/	.1011 20100000 110	
		1	ence as set forth	
	in Figure 1 (S	/		
25		mi/no acid sequenc	e of subpart (a)	
		rent amino acid s		
	deleted in one	or more of the f	following positions	
	(using the num	bering according	to Figure 1):	
	(i)	one or more cyst	eine residues;	
30	(i / i)	one or more tyro	sine residues;	
	(fiii)cysteine at posi	tion 5 deleted or	
	substitute¢ wi			
	/		cion 20 deleted or	
	substituted wi		4.00	
35	1	glutamic acid at		
	deleted/or sub	stituted with an	alanine;	

	(vi) lysine at position 105 deleted or
	substituted with an alanine;
	(vii)lysine at position 107 deleted or
	substituted with an alanine;
5	(viii)deletion or substitution of one or
	more of the amino acids at positions 1, 2, 3, 4,
	and 5;
	(ix) one or more residues substituted or
	deleted to ablate the Fc receptor binding site;
10	(x) one or more residues substituted or
	deleted to ablate the complement (C1q) binding
	site; and
	(xi) a combination of subparts i-x;
	(c) the amino acid sequence of subparts (a)
15	or (b) having a methiony residue at the
	N-terminus;
	(d) the Fc protein, or variant, fragment or
	derivative thereof, of any of subparts (a) through
	(c) comprised of a chemical moiety connected to
20	the protein moiety;
	(e) a defivative of subpart (d) wherein said
	chemical moiety is a water soluble polymer moiety;
	(f) a derivative of subpart (e) wherein said
	water soluble polymer moiety is polyethylene
25	glycol; and /
	(g) a deriyative of subpart (e) wherein said
	water soluble polymer moiety is attached at solely
	the N-terminus of said protein moiety.
30	10. The nucleic acid sequence according to
	claim 8 encoding for a protein comprising an OPG
	protein, variant / fragment or derivative portion
	selected from the group consisting of:
	(a) the amino acid sequence 22-X wherein X

is any residue from position 185 to 401 inclusive

as shown in Figure 2 (SEQ ID NO: <u>\(\frac{1}{2}\)</u>);

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- (b) the amino acid sequence 22-X wherein X is any residue from position 185 to 293 inclusive as shown in Figure 2 (SEQ ID NO: 2);
- (c) the amino acid sequence of subparts (a)
 and (b) having a methionyl residue at the
 N-terminus;
- (d) the OPG protein, or variant, fragment or derivative thereof, of any of supparts (a), (b) and(c) comprised of a chemical moiety connected to the protein moiety;
- (e) a derivative of subpart (d) wherein said chemical moiety is a water soluble polymer moiety;
- (f) a derivative of subpart (e) wherein said
 water soluble polymer moiety is polyethylene
 glycol;
- (g) A derivative of subpart (e) wherein said water soluble polymer moiety is a polyamino acid moiety; and
- (h) a derivative of subpart (e) wherein said 20 water soluble polymer moiety is attached at solely the N-terminus of said protein moiety.
- 11. The nucleic acid sequence of claim 8 encoding for a protein comprising a linker of one or 25 more amino acids selected from the group consisting of glycine, asparagine, seripe, threonine and alanine.
- 12. The nucleic acid sequence of claim 8 encoding for a protein with a linker selected from the 30 group consisting of:
 - (a) ala-ala-ala;
 - (b) #la-ala-ala-ala;
 - (c) /ala-ala-ala-ala;
 - (d) / gly-gly;
- $f(e) = \int gly-gly-gly;$
 - (f) / qly-gly-gly-gly;

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- gly-gly-gly-gly-gly/gly; (g)
- gly-pro-gly; (h)
- gly-gly-pro-gly-gly; (i)
- (j) val;
- ser-gly-gly-gly-gly-gly-gly-(k)

- gly-gly-ser-gly-ser-gly-ala-gly-(1) ser-gly-ser-gly-gly-ser-gly-ser-gly;

 - (m) a chemical moietly; and
 - any combination of subparts (a) (n)

through (m).

- A nucleic acid sequence encoding a 13. fusion protein comprising the amino acid sequence selecting from the group consisting of: the amino acid 15 sequences as set forth in Figures 5, 6, 7 or 8 (SEQ ID NOS: 5, μ , 7, 8 respectively).
- A/wector comprising a nucleic acid sequence according to any of Claims 8 to 13 inclusive. 20
 - A prokaryotic or eukaryotic host cell 15. containing the vector of claim 14.
- A process for producing a protein of 25 claims 1 or 6 comprising the steps of culturing, under suitable conditions, the host cell of claim 15, and isolating the protein produced.
- The/process of claim 16 further 30 17. comprising the step of purifying the protein produced.
- A pharmaceutical composition comprising 18. an effective amount of a protein according to claims 1 or 6, in a pharmaceutically acceptable diluent, 35 adjuvant or ¢arrier.

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19. A method of preventing or treating a bone loss in a mammal comprising administering a therapeutically effective amount of the protein of any of Claims 1-6.

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The method of Claim 19 wherein the bone loss is selected from the group consisting of osteoporosis, Paget's disease, osteomyelitis,

hypercalcemia, osteopenia associated with surgery or 10 steroid administration, osteonecrosis, bone loss due to rheumatoid arthritis, periodontal bone loss, osteolytic metastasis, and prosthetic loosening.